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Decreased latencies for limbic seizures induced in rats by lithium-pilocarpine occur when daily average geomagnetic activity exceeds 20 nanoTesla

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Abstract

A decrease in the latency for the overt display of limbic seizures following the systemic injection of lithium and pilocarpine is weakly associated with enhanced global geomagnetic activity (in nanoTesla; nT). To determine the optimal threshold in global geomagnetic activity that is required for this effect, the seizure onset times for over 300 rats were dichotomized according to successive 5 nT increments. The results suggested that the seizure process occurred about 12% more quickly when the average daily global geomagnetic activity exceeded 20–25 nT and is commensurate with the observations by other researchers.

Keywords: Geomagnetic activity; Threshold; Limbic seizures; Rats; Epilepsy

Field observations have strongly suggested that alterations in complex behaviors that involve spatial orientation or memory, occur when the average geomagnetic activity exceeds values of between 10 and 30 nanoTesla (nT) [1,5,11,20]. Electrical lability, which can be inferred from the rates of epileptic convulsions, increases during days [3,9] or months [17] when the average geomagnetic activity exceeds about 30 nT. The threshold for experiences that are strongly correlated with paroxysmal discharges within the hippocampal-amygdaloid complex may be between about 20 and 30 nT [14,18]. During vulnerable periods, such as birth, concurrent activity that exceeds 20–30 nT may be associated with permanent alterations in limbic sensitivity [6].

Like other researchers, we have suspected that: (a) the effect of geomagnetic activity upon the electrical lability of the limbic system is non-linear; and hence (b) a limen (threshold) should exist. If we applied a successive increment method, then there should be some intensity value that would produce the largest effect size between seizure onset times below and above this threshold and, simultaneously, the smallest discrepancy in the variances between the 2 groups. Because the total sample would remain the same with this procedure, the strength of the effect would be more revealing than the level of statistical significance. With concomitant consideration of heterogeneity of variance between the successive dichotomies, potential confounds from asymmetric sample sizes would be reduced.

To test this hypothesis we obtained the seizure onset times for all of the 317 male Wistar albino rats, in which limbic seizures had been induced in our laboratory, for 15 successive months that included January 1993 through March 1994. During this period, observations had been made on 62 different days (between 3 and 6 observations per month); between 2 and 8 rats had been observed on any given day.

All rats had received food and water ad libitum and had been maintained in temperature controlled rooms in a 12 h light/dark cycle (local night beginning 1930 h). The subjects were between 90 and 130 days of age when 3 mEq of lithium chloride had been injected s.c. between 1200 and 1300 h local time, followed by 30 mg/kg s.c. of pilocarpine 4 h later [2,3]. The latency (min) before the onset of forepaw clonus was recorded.

The global daily geomagnetic activity (nT) for the northern hemisphere (Geomagnetic Indices Bulletin, National Geophysical Data Center, Solar-Terrestrial Physics

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Division, 325 Broadway, Boulder, CO 80303) was obtained for the day, and for each of the three days before and after, the seizures had been induced. Only the 24 h geomagnetic activity for the days in which the seizures had been induced was significantly associated with the seizure onset times. The results are shown in Table 1 where the numbers of rats and the means and standard deviations for the seizure onset times below or above successive increments of 5 nT or 10 nT were determined.

The results confirmed the hypothesis. Rats displayed significantly faster seizure onset times when the daily global geomagnetic activity exceeded 20 nT, relative to those rats in which seizures were induced when the activity was below this value. The optimal dichotomy of the seizure onset times, as determined by effect size and the minimum heterogeneity of variance was 25 nT. One-way analyses of variance for the square-root transformations of the seizure onset times verified the significantly faster seizure onset times when the geomagnetic activity was equal to or exceeded 25 nT ($F(1,315) = 11.63$, $P < 0.001$); there was minimum heterogeneity of variance (Bartlett's Box, 5.90; $P > 0.01$). No other dichotomy satisfied both of the criterion for the indices of central tendency and dispersion.

Non-parametric analysis of variance (Kruskal–Wallis) demonstrated that the only significant group differences occurred for dichotomies where the limen was set at 20 nT (chi-squared, 5.84; $P < 0.01$), 25 nT (chi-squared, 9.74; $P < 0.001$) or 30 nT (chi-squared, 3.95; $P = 0.05$). For reference, the mean and standard deviation for the daily geomagnetic activity in the northern hemisphere, for the days on which the seizures were induced for the total population, were 36.8 nT and 21.7 nT (range, 8–93 nT), respectively. The values for the monthly averages were 31.8 nT and 8.4 nT, respectively.

The effect size of the relationship between enhanced geomagnetic activity (over 20 nT) and the faster onset of overt limbic seizures was equivalent to a correlation coefficient of about 0.20. Recalculation of previous data [10] concerning bereavement hallucinations and concurrent geomagnetic activity demonstrated an eta value of about 0.30. The magnitude and the timing of the facilitation of the seizure process that was observed in this study support our hypothesis that geomagnetic activity-induced suppression of circulating melatonin during the concurrent 24 h period may be significantly involved with the lowered seizure thresholds.

Table 1

Number of subjects (N), mean seizure onset time (M; min) and the standard deviations (SD) as a function of days below or above successive dichotomies of geomagnetic activity (eta refers to equivalent correlation coefficient).

Limit (nT)	Below			Above			eta
	N	M	SD	N	M	SD	
15	43	29.7	10.7	274	30.3	9.5	0.05
20	74	33.0[a]	12.2[a]	243	29.3[b]	8.6[c]	0.16*
25	116	32.7[a]	11.1[a]	201	28.8[c]	8.4[c]	0.20**
30	142	31.5[a]	10.9[a]	175	29.1[b]	8.4[c]	0.12*
35	159	31.2	10.6[a]	158	29.3	8.6[b]	0.10
40	189	31.3[a]	10.9[a]	128	28.6[b]	7.0[c]	0.15
50	247	30.6	10.2[a]	70	28.9	7.2[c]	0.06
60	270	30.7	10.0[a]	47	27.9	6.7[c]	0.07

[a] versus [b], $P < 0.05$; [a] versus [c], $P < 0.001$; *$P < 0.05$, Kruskal–Wallis; **$P < 0.001$, Kruskal–Wallis.

Although whole body exposure to more intense (μT) magnetic fields have been required to evoke statistically significant depletions in melatonin [19], the exposure duration is usually much shorter (e.g. about 1 h) compared to natural settings. A recent study [15] demonstrated that the proportion of chronic epileptic rats that exhibited overt seizures per day increased (over 90 successive days) when the concurrent 3 h geomagnetic activity and the activity during the previous mid-scotophase (0200–0600 h) exceeded 30 nT. These results indicated that increased geomagnetic activity during the previous 24 h encouraged overt motor automatisms in response to environmental events (e.g. synchronized feeding) whose neurochemical correlates (e.g. corticotrophin releasing factor; CRF) are epileptogenic.

Direct application of still weaker (pT) magnetic fields, with a band width of 2–7 Hz, directly over the pineal organ of human epileptics, has been shown [7] to be associated with alterations in melatonin production. Although the mechanism by which the actual transduction of geomagnetic activity into neural activity must be verified experimentally, the hypothesis by Lerchl et. al. [10] is promising. They argue that electric eddy currents, whose peak-to-peak variations are in the order of seconds, are generated by increases and decreases in geomagnetic activity. Intricate neuronal networks [16] that occur uniquely within the pineal organ may determine its sensitivity.

There is a persistent vectorial reversal that differentiates correlational and experimental research with extremely low frequency magnetic fields. Whereas thresholds for electrical seizures decrease (and overt symptoms increase) during periods of enhanced geomagnetic activity, almost all experimental exposures are associated with observations that suggest increased thresholds [8,12,13]. Recently, we [4] administered subclinical injections of lithium (1.5 mEq/kg) and (4 h later) pilocarpine (15 mg/kg) to rats every second day for 40 days; after each pilocarpine injection, the rats were exposed for 4 min to 5 μT, pulsed fields in order to 'kindle' the seizures; however significant inhibition was also found. It is possible that weaker (nT) fields whose amplitudes vary over minutes for several hours, thus simulating geomagnetic activity, may be required to resolve this disparity.

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